REMARKS

Reconsideration of the rejections set forth in the Office Action dated July 18, 2001 is respectfully requested. Applicant petitions the Commissioner for a 1-month extension of time. A separate petition accompanies this amendment. Claims 1-9 are currently under examination.

I. Amendments

The specification has been amended to correct minor typographical errors. The claims have been amended as set forth above. Support for the definition of *i* in claim 1 can be found in at least Fig. 3. Support for the amendment reciting that the protein not be in a coiled-coil configuration in its native state can be found on at least page 17, lines 28-31 of the specification.

Attached is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

No new matter has been added by these amendments.

II. Rejection Under 35 U.S.C. §112, second paragraph

Claims 1-9 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. This rejection is traversed in view of the following.

Claim 1 was rejected in view of the recitation of the phrase "n is at least three". The Examiner's position is that it is not clear if n is infinite or any number in between three and infinity.

Applicants contend that the phrase is clear and definite. The term "at least" coupled with the specific number three is a lower limit of a range (i.e., 3 on up). Two Federal Circuit cases have held similar phrases to be in accordance with Applicants' definition.

The Federal Circuit interpreted a claim reciting "at least two conveyors" to require two or more separate conveyers. As stated by the court, "When claiming a combination where more than one of a certain element, here a conveyor [means], is included in the combination, the term "at least two" sets forth the minimum number of a particular element required." *Lantech Inc. v. Keip Mach. Co.* 32 F.3d 542, 31 USPQ 2d 1666, 1670 (Fed. Cir. 1994).

The Federal Circuit defined the term "at least 600" to mean an open-ended range starting slightly below 600 in *Quantum Corp. v. Rodime, PLC* 65 F.3d 1577, 36 USPQ 2d 1162 (Fed. Cir. 1995), *cert. denied*, 517 U.S. 1167 (1996). Regarding the limitation "at least 600," the Federal

Circuit, using Webster's Dictionary, interpreted the term "at least" to mean "as the minimum." The Federal Circuit interpreted the term "at least" coupled with a specific number in the claim limitation as a lower limit of a range (i.e., 600 on up).

Claim 1 has been amended to define *i* as equal to 1, 2, ..., *n*.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

III. Rejection under 35 U.S.C. §102(e)

Claims 1-5 were rejected under 35 U.S.C. §102(e) as being anticipated by Anderson (U.S. Patent No. 6,242,213 B1). This rejection is respectfully traversed in view of the foregoing claim amendments and following remarks.

A. The Claimed Invention

The present invention, as embodied in amended claim 1, is directed to a coiled-coil polypeptide composition comprising a template of the form $(ab_ic_id_ie_if_ig_i)_n$, where the sequence formed by the positions $(b_ic_ie_if_ig_i)_n$ is a sequence of amino acids from a solvent-accessible region of an epitope from a selected protein, where the region is not in a coiled-coil conformation in its native state.

B. The Prior Art

Anderson discloses isolated DNA molecules encoding RANK-L, and briefly describes leucine zipper domains and proteins that form coiled-coil dimers in their native state (column 6, lines 63-65. Nowhere does Anderson show or suggest a coiled-coil composition comprising a template of the form $(ab_ic_id_ie_if_ig_i)_n$, where the sequence formed by the positions $(b_ic_ie_if_ig_i)_n$ is a sequence of amino acids from a solvent-accessible region of an epitope from a selected protein, where said region is not in a coiled-coil conformation in its native state.

C. Analysis

For a prior art reference to be anticipating under 35 U.S.C. §102(b), it must teach "each and every" element of the claimed invention. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). "Anticipation requires identity of invention: the claimed invention, as described in appropriately construed claims, must be the same as that of the reference, in order to anticipate." *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.*, 33 USPQ2d 1496 (Fed. Cir. 1995).

The present invention as claimed recites the elements indicated in Section III. A. As discussed above in Section III. B., Anderson does not disclose or suggest a composition comprising a template where the sequence formed by certain positions is an amino acid sequence from a region of a protein that is not in a coiled-coil conformation in its native state. Therefore, Anderson cannot anticipate the claimed invention under 35 USC 102(e).

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102(e).

IV. Rejection Under 35 U.S.C. §103

Claims 1-9 were rejected under 35 U.S.C. §103(a) as being obvious over Anderson (U.S. Patent No. 6,242,213 B1) in view of Prusiner *et al.* (U.S. Patent 5,792,901). This rejection is respectfully traversed for the following reasons.

A. The Present Invention

The invention is described above. Although there has been considerable interest in preparing compositions capable of mimicing or blocking conformationally distinct protein-protein interactions in cells, and for generating antibodies capable of recognizing distinct protein conformations, the tools necessary to achieve this preparation have not been available. The present invention addresses this problem, and solves it by inserting solvent-accessible residues of an epitope from a region of a protein that is normally not in a coiled-coil conformation into a conformationally-restricted, stabilized coiled-coil template.

B. The Cited Art

Anderson is described above. The reference is not concerned with the problem addressed by the present invention, nor does it suggest Applicants' solution. In particular, the reference does not show or suggest inserting solvent-accessible residues of an epitope from a region of a protein that is normally not in a coiled-coil conformation into a conformationally-restricted, stabilized coiled-coil template.

Prusiner *et al.* describe a transgenic animal containing an artificial prion protein. Prusiner *et al.* is not concerned with the problem addressed by the present invention, nor does the reference suggest Applicants' solution for the same reasons as were applied to Anderson.

C. Analysis

C1. Legal Standard for Nonobviousness.

In determining whether an invention is nonobvious, the PTO has the burden of establishing a case of *prima facie* obviousness. A proper analysis under 35 U.S.C. §103 requires consideration of whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process and whether the prior art would have also revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. See MPEP §2142, citing *In re Vaeck,* 20 USPQ2d 1438, Fed. Cir. 1991.

Thus, for a combination of references to render a claimed invention obvious under 35 U.S.C §103, that combination must provide not only a suggestion of the present invention, but also a reasonable expectation of success in reaching that invention. Under these standards, and as discussed below, the Examiner has not made a *prima facie* case of obviousness.

C2. Lack of suggestion in the prior art

In order for the prior art to provide motivation for combining references along the lines of the invention, the prior art must recognize the advantages to be gained by such combination. As noted above, none of the references cited is concerned with the problem of preparing compositions capable of mimicing or blocking conformationally distinct protein-protein interactions in cells, or for generating antibodies capable of recognizing distinct protein conformations. Nor do either of the references suggest the possibility of addressing the problem successfully by inserting solvent-accessible residues of an epitope from a region of a protein that is normally not in a coiled-coil conformation into a conformationally-resticted, stabilized coiled-coil template.

The Examiner points to column 6, lines 17-18 of Prusiner *et al.* as providing the motivation necessary to achieve the present invention. However, the paragraph beginning on column 6, lines 17-18 is concerned with testing samples for the presence of prions by creating two groups of non-human mammals which have their genome altered so that they are susceptible to infection with prions which generally only infect a genetically diverse animal. The reference provides no suggestion or motivation for inserting the solvent-accessible amino acid residues of the prion protein into a conformationally-restricted, stabilized coiled-coil template.

In the absence of such a suggestion, and failing to recognize the problem addressed by the present invention, and its solution, the prior art cannot be said to provide a suggestion or

motivation for the claimed invention. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103(a).

V. Conclusion

In view of the above remarks, the applicants submit that the claims now pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,

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Date: 11-14-01

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at line 10 of page 5 has been amended as follows:

"Epitope" as used herein describes the amino acid component of a molecule and the structural component of a molecule that is responsible for specific interactions with corresponding antibody (immunoglobulin) molecules elicited by the same or related antigen. Epitopes can be either linear [of] or conformational. Linear epitopes refer to contiguous amino acid residues in a sequence whereas conformational epitopes are formed from non-contiguous amino acids in the sequence and are dependent on both the secondary and tertiary structure of the molecule.

The paragraph beginning at line 16 of page 15 has been amended as follows:

Current detection methods for PrP^{C} and PrP^{SC} rely on polyclonal and monoclonal antibodies which recognize both forms of PrP. Most antibodies in the prior art to date are directed against linear epitopes which are present in both denatured PrP^{C} and PrP^{SC}. In order to distinguish between PrP^{C} and PrP^{SC} it is therefore necessary to utilize a procedure involving protease treatment followed by immunodetection on Western blots. While PrP^{C} is degraded by proteolysis, PrP^{SC} is largely resistant to proteolysis and gives a signature set of undigestable products PrP27-31 which can then be detected by immunodetection. Since these antibodies only recognize denatured forms of PrP, they can only be used to detect PrP under denaturing conditions such as those used for immunohistology or to detect PrP in extracts from various tissues or fluids. In order to carry out assays for native forms of PrP^{C} and PrP^{SC}, it is necessary to develop ligands which will selectively recognize the respective forms of these proteins.

The paragraph beginning at line 11 of page 16 has been amended as follows:

The H3 heterodimer construct (Fig. 4B) was conjugated to [kehyole] keyhole limpet hemocyanin (KLH) and to bovine serum albumin, as described in Example 1A. The KLH-polypeptide conjugate in the presence of Freund's adjuvant was injected into rabbits according to the procedure outlined in Example 1B. Each test animal received a first injection of the KLH-polypeptide in Freunds's Complete adjuvant, followed two weeks later with a second injection of the KLH-polypeptide conjugate in Freund's Incomplete adjuvant. Two weeks after the second injection, the serum antibody titer was determined using ELISA, as described in Example 1C.

In the Claims:

Claim 1 has been amended as follows:

1. (Amended) A coiled-coil polypeptide composition, comprising

a template of the form $(ab_ic_id_ie_if_ig_i)_n$, where i=1,2,...,n, and n is at least three, *a* and *d* are amino acids selected from the group consisting of leucine, isoleucine, valine, phenylalanine, methionine, tyrosine, and derivatives thereof, and the sequence formed by the positions $(b_ic_ie_if_ig_i)_n$ is a sequence of amino acids from a solvent-accessible region of an epitope from a selected protein, where said region is not in a coiled-coil conformation in its native state.